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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,615	12/26/2001	Paul Meers		9551

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EXAMINER

KISHORE, GOLLAMUDI S

ART UNIT PAPER NUMBER

1615

DATE MAILED: 07/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/914,615

**Applicant(s)**

MEERS ET AL.

**Examiner**

Gollamudi S. Kishore, Ph.D

**Art Unit**

1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 18 April 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-4 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |                                                                                                                        |                                                                                         |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____                                                |

### DETAILED ACTION

The RCE filed on 4-18-05 is acknowledged.

Claims included in the prosecution are 1-4.

#### *Claim Rejections - 35 USC § 102*

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

2. Claims 1, 3 and 4 are rejected under 35 U.S.C. 102(a) as being anticipated by Kim (5,723,147).

Kim discloses a process of preparation of liposomes in which the lipid in an organic solvent is added with an aqueous solution of an active agent, which in turn is added, with a second aqueous solution containing lysine. The organic solvent is then removed. Kim teaches various active agents including DNA and RNA (abstract, col. 6, line 62 and Examples). Instant claims do not recite specific complexing agents and the nature of complexing, i.e., whether it is ionic or covalent. Since anions and cations are known to interact to form complexes and since Kim teaches both anionic and cationic active agents (morphine, morphine sulfate and nucleic acids), they would naturally be complexing with lysine (free base) or lysine hydrochloride. The reference thus, meets the requirements of instant claims.

Art Unit: 1615

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that lysine in Kim is used to control pH and the role of the complexing agent in the present application is described on page 16, lines 11-15 of the specification. These arguments are not found to be persuasive. The limitations argued by applicant are not present in the claims. According to the definition on page 16, lines 11-15, bioactive complex should have one of the properties listed and among the properties listed is "increasing the size of the complex". Since the addition of lysine to any active agent would increase the size of the complex of that active agent, Kim meets the requirements of instant claims. Claims are given the broadest reasonable interpretation and as pointed out before, instant claims do not recite specific complexing agents and therefore, lysine in the prior art meets the requirements of the complexing agents irrespective of the purpose for which it is used in the prior art. The rejection is maintained.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Kim (Cancer Research 53, pp. 1596-1598, April 1993).

Kim discloses a process of preparation of liposomes in which the lipid in an organic solvent is added with an aqueous solution of an active agent, which in turn is added, with a second aqueous solution containing lysine. The organic solvent is then removed (Materials and Methods section on col. 2, page 1596).

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant's arguments are similar to those advanced for Kim, 147. Since the methodology in both Kim's references is the same, the same response as above is applicable. Applicant further argues that the role of HCl is to lower the pH to such a degree that every available Lewis base is either neutral or cationic. In such an environment according to applicant there would be no complexing occurring. This argument is not persuasive. According to applicants own statement the Lewis base either neutral or **cationic**. That means the cationic species is able to react with an anionic species to form a complex.

*Claim Rejections - 35 USC § 103*

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kim (5,723,147) cited above.

The teachings of Kim have been discussed above. Kim does not teach the addition of the complexing agent to the lipid solution first followed by the addition of the active agent solution. Since complexing occurs between the active agent and the complexing agent irrespective of which one is added first, instant method steps are deemed to be manipulatable steps practiced by an artisan.

Applicant's arguments have been fully considered, but are not found to be persuasive, Applicant argues that Kim first reacts the bioactive agent with cyclodextrin in an aqueous phase and this aqueous phase is then added to the lipid-chloroform solution and that this is different from the present claimed methods. This argument is not found to be persuasive since instant claims neither define the bioactive agent nor exclude cyclodextrin in the prior art. As pointed out above, since the complex is formed between lysine and the active agent, irrespective of which is added first. Applicant's arguments with regard to the physical properties such as the precipitation of the complex as discussed in the specification have been addressed above.

6. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim **(5,759,573)**.

Instant method claims are drawn to formation of liposomes wherein the active agent is complexed with a complexing agent; the method steps in claims 1 and 2 recite two variables. 1) the complexing agent is added in the second aqueous solution whereas the active agent is added in the first aqueous phase (claim 1); 2) the complexing agent is added in the first aqueous medium and the active agent is added in the second aqueous medium.

Kim discloses a process of preparation of liposomes in which the lipid in an organic solvent is added with an aqueous solution of an active agent, which in turn is added, with a second aqueous solution. The organic solvent is then removed. In Kim's process, the complexing agent, cyclodextrin is added in the first aqueous phase together with the active agent (col. 4, lines 13-26 and Example 1).

Art Unit: 1615

However, it would have been obvious to one of ordinary skill in the art to manipulate the basic process of preparation of liposomes, i.e., adding the complexing agent and the active agent together in the same aqueous medium with the expectation of obtaining liposomes with similar complexes because one of ordinary skill in the art would reasonably expect the complexation between the active agent and the complexing agent to occur, irrespective of whether they are added together in the same phase or separately in two phases. Kim does not specifically teach the active agent to be a nucleic acid. However, in view of Kim's teachings that the method is applicable to any active agent, it is deemed obvious to one of ordinary skill in the art to use DNA or RNA as the active agent with a reasonable expectation of success.


Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant's arguments are similar to those advanced for the other rejections over Kim's references. These have been addressed above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1615

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Gollamudi S Kishore, Ph.D  
Primary Examiner  
Art Unit 1615

GSK